# Integrated Efficacy of FMX101 4% Topical Minocycline Foam for the Treatment of Moderate-to-Severe Acne Vulgaris: Analyses of Efficacy in Clinically Relevant Subgroups of Patients

James Q. Del Rosso, DO[1], Linda Stein Gold, MD[2], Leon Kircik, MD[3], Andrew Alexis, MD[4], Seemal R. Desai, MD[5,6], Vassilis Stakias, PharmD[7], Iain Stuart, PhD[7]

[1]JDR Dermatology Research/Thomas Dermatology, Las Vegas, NV; [2]Henry Ford Health System, Detroit, MI; [3]Icahn School of Medicine at Mount Sinai, New York, NY; [4]Mount Sinai, New York, NY; [5]Innovative Dermatology, Plano, TX; [6]Department of Dermatology, The University of Texas Southwestern Medical Center, Dallas, TX; [7]VYNE Therapeutics Inc., Bridgewater, NJ

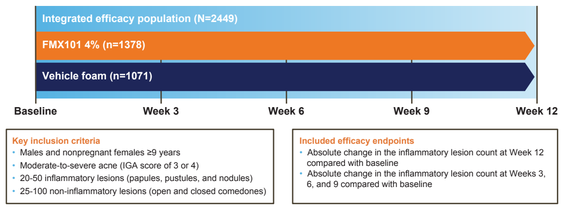
## Introduction

- Acne vulgaris is a chronic, inflammatory skin disorder that affects most of the population at some point in their lifetime[1]
- Oral minocycline and doxycycline are considered first-line therapy for the treatment of moderate-to-severe acne, but they are associated with potentially serious systemic side effects[2]
- FMX101 4% is the first stable, topical foam formulation of minocycline and has been FDA-approved for the daily treatment of acne
- The efficacy of FMX101 4% in treating acne has previously been demonstrated in 3 double-blind, vehicle-controlled, 12-week, Phase 3 clinical trials (FX2014-04, FX2014-05, and FX2017-22)[3-4]
- **Objective:** To provide an integrated summary of efficacy of FMX101 4% versus vehicle foam for a pooled population of ~2500 subjects and for predefined subgroups of subjects that differ according to baseline disease severity, sex, age, and race

## Methods

- The 3 pivotal Phase 3 studies (FX2014-04, N=466; FX2014-05, N=495; and FX2017-22, N=1488) were randomized, double-blind comparisons of FMX101 4% to vehicle foam (**Figure 1**)
- Data for the change in inflammatory lesions from baseline at Weeks 3, 6, 9, and 12 were pooled for overall analysis and for analysis of predefined subgroups that were separated by baseline disease severity (moderate, IGA=3, or severe, IGA=4), sex (male or female), age group (9-17 or ≥18 years) and race (white or non-white)

### Figure 1. Study design




**Key inclusion criteria**
- Males and nonpregnant females ≥9 years
- Moderate-to-severe acne (IGA score of 3 or 4)
- 20-50 inflammatory lesions (papules, pustules, and nodules)
- 25-100 non-inflammatory lesions (open and closed comedones)

**Included efficacy endpoints**
- Absolute change in the inflammatory lesion count at Week 12 compared with baseline
- Absolute change in the inflammatory lesion count at Weeks 3, 6, and 9 compared with baseline

IGA, Investigator's Global Assessment, based upon a 6-point scale in which 0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe, and 5=very severe.

## Results

### Baseline Demographics and Disease Characteristics

- Baseline demographics and disease characteristics were similar across treatment groups (**Table 1**)
- Overall, the majority of subjects were female (60.6%) and white (73.1%) with moderate baseline disease severity (85.0%)
- Similar proportions of the subjects were pediatric (9-17 years, 48.4%) or adult (≥18 years, 51.6%)

### Table 1. Baseline demographics and disease characteristics

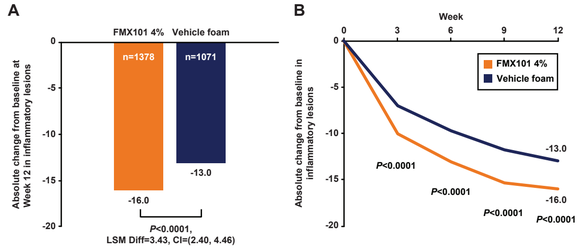
| Variable | FMX101 4% (n=1378) | Vehicle foam (n=1071) | Overall (N=2449) |
|---|---|---|---|
| **Age** | | | |
| 9 to 17 years, n (%) | 670 (48.6) | 515 (48.1) | 1185 (48.4) |
| ≥18 years, n (%) | 708 (51.4) | 556 (51.9) | 1264 (51.6) |
| **Sex, n (%)** | | | |
| Male | 553 (40.1) | 411 (38.4) | 964 (39.4) |
| Female | 825 (59.9) | 660 (61.6) | 1485 (60.6) |
| **Race, n (%)** | | | |
| White | 1006 (73.0) | 784 (73.2) | 1790 (73.1) |
| Non-white | 372 (27.0) | 287 (26.8) | 659 (26.9) |
| Black or African American | 283 (20.6) | 213 (19.9) | 496 (20.3) |
| Asian | 54 (3.9) | 46 (4.3) | 100 (4.1) |
| American Indian or Alaska Native | 1 (0.1) | 3 (0.3) | 4 (0.2) |
| Native Hawaiian or Other Pacific Islander | 3 (0.2) | 3 (0.3) | 8 (0.3) |
| More than one race | 30 (2.2) | 19 (1.8) | 49 (2.0) |
| **Inflammatory lesion count, mean (SD)** | 31.2 (8.65) | 31.1 (8.31) | 31.2 (8.50) |
| **IGA score, n (%)** | | | |
| 3 – Moderate | 1171 (85.0) | 911 (85.1) | 2082 (85.0) |
| 4 – Severe | 207 (15.0) | 160 (14.9) | 367 (15.0) |

IGA, Investigator's Global Assessment.

### Efficacy of FMX101 4% in the Pooled Population

- Overall, in the combined analysis of the 3 pivotal Phase 3 studies, FMX101 4% demonstrated statistically significant benefit compared with vehicle foam
  - FMX101 4% demonstrated a significantly greater reduction from baseline in inflammatory lesions at Week 12 than vehicle foam (**Figure 2A**)
  - Statistically significant advantages of FMX101 4% over vehicle foam were observed as early as Week 3, and were sustained throughout the treatment period (**Figure 2B**)

### Figure 2. Absolute reduction from baseline in inflammatory lesions for the pooled population

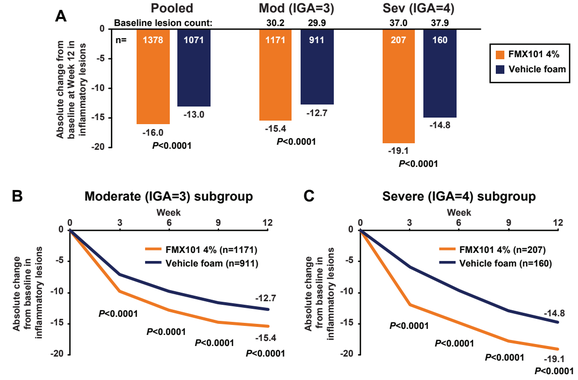



LSM Diff, least squares mean difference; CI, confidence interval; ITT population with multiple imputation; *P* values are based on LSM Diff from ANCOVA.

### Reduction in Inflammatory Lesions by Baseline Disease Severity

- FMX101 4% demonstrated a statistically significant advantage over vehicle foam at Week 12, irrespective of baseline disease severity (**Figure 3A**)
- In the FMX101 4% group, there was a significantly greater reduction in inflammatory lesions from baseline compared with vehicle as early as Week 3 that was maintained throughout treatment in both moderate (**Figure 3B**) and severe (**Figure 3C**) subgroups

### Figure 3. Efficacy of FMX101 4% across baseline disease severities

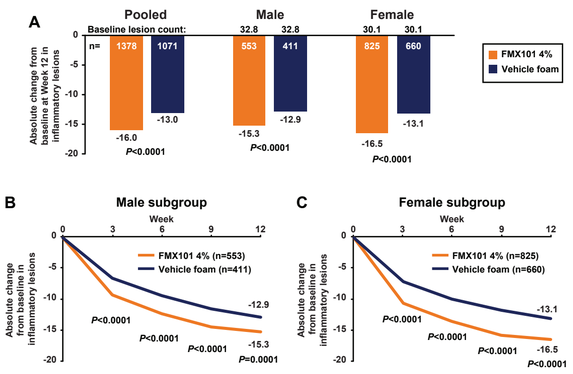



Mod, moderate; Sev, severe; ITT population with MI; *P* values are based on LSM Difference from ANCOVA.

### Reduction in Inflammatory Lesions by Sex

- In both male and female subpopulations, FMX101 4% exhibited significantly greater reductions in inflammatory lesions at Week 12 compared with vehicle foam (**Figure 4A**)
- The time course of efficacy of FMX101 4% over vehicle foam was comparable between sexes, with statistically significant advantages of FMX101 4% over vehicle observed at Week 3 and maintained throughout study treatment (**Figure 4B-C**)

### Figure 4. Reduction in inflammatory lesions for sex subgroups

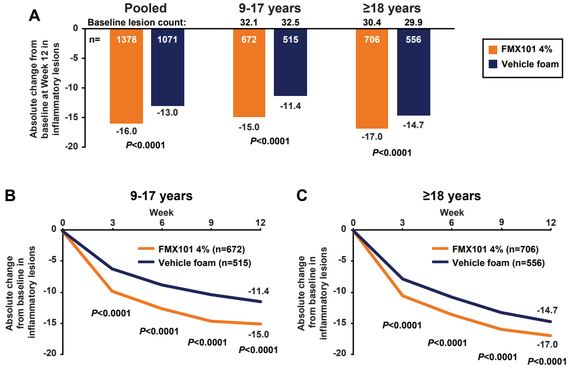



ITT population with MI; *P* values are based on LSM Difference from ANCOVA.

### Reduction in Inflammatory Lesions by Age

- FMX101 4% exhibited significantly greater reductions in inflammatory lesions at Week 12 compared with vehicle foam regardless of age subgroup (**Figure 5A**)
- The time course of efficacy of FMX101 4% over vehicle foam was comparable between pediatric (<18 years old) vs adults (≥18 years old), with statistically significant advantages of FMX101 4% over vehicle observed at Week 3 and maintained throughout study treatment (**Figure 5B-C**)

### Figure 5. Reduction in inflammatory lesions for age subgroups

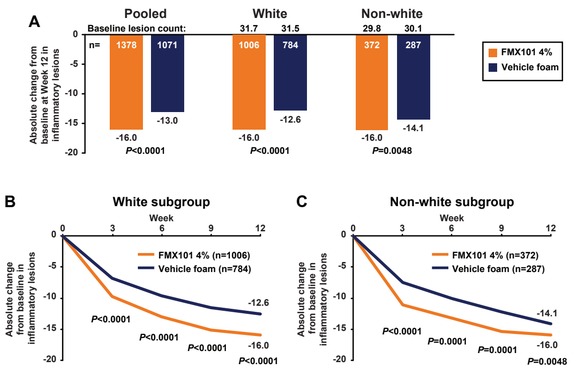



ITT population with MI; *P* values are based on LSM Difference from ANCOVA.

### Reduction in Inflammatory Lesions by Race

- In both white and non-white subjects, FMX101 4% exhibited significantly greater reductions in inflammatory lesions at Week 12 compared with vehicle foam (**Figure 6A**)
- Statistically significant advantages of FMX101 4% over vehicle foam were observed as early as Week 3, and were sustained throughout the treatment period for both white (**Figure 6B**) and non-white (**Figure 6C**) subgroups

### Figure 6. Reduction in inflammatory lesions for race subgroups




ITT population with MI; *P* values are based on LSM Difference from ANCOVA.

## Summary

- FMX101 4% demonstrated efficacy over vehicle foam in treating moderate-to-severe acne vulgaris in a pooled population of ~2500 subjects from 3 Phase 3 studies
  - Overall, the FMX101 4% group exhibited a significantly greater reduction in inflammatory lesions from baseline at Week 12 compared with the vehicle group
  - Efficacy of FMX101 4% over vehicle foam was observed as early as Week 3, and continued throughout the 12-week treatment period
- Analyses were performed on the integrated data set to characterize the efficacy of FMX101 4% in treating acne in predefined subgroups of subjects
  - Consistent with results from the pooled population, FMX101 4% resulted in significantly greater reductions in inflammatory lesions at all assessed timepoints in subgroups of subjects that were separated by baseline disease severity, sex, age, and race

## Conclusions

- FMX101 4% demonstrated statistically significant differences compared with vehicle in the reduction of inflammatory lesions from baseline at Weeks 3, 6, 9, and 12 in a pooled population of 3 Phase 3 studies, as well as in predefined subgroups of subjects
- These data suggest that FMX101 4% appears to be effective for the treatment of acne in a wide variety of patients, whether male or female, adult or pediatric, white or non-white, and with moderate or severe disease at baseline

## Disclosures/Acknowledgment

**Disclosures**
**Dr. Del Rosso** is a consultant for Aclaris, Almirall, Athenex, Cutanea, Dermira, Ferndale, Galderma, Genentech, LEO Pharma, Menlo, Novan, Ortho, Pfizer, Promius, Sanofi/Regeneron, SkinFix, and SunPharma; he has received research support from Aclaris, Almirall, Athenex, Botanix, Celgene, Cutanea, Dermira, Galderma, Genentech, LEO Pharma, Menlo, Novan, Ortho, Promius, Regeneron, SunPharma, and Thync; he receives honoraria from Aclaris, Celgene, Galderma, Genentech, LEO Pharma, Novartis, Ortho, Pfizer, Promius, Sanofi/Regeneron, and SunPharma; and he participates in speakers bureaus for honoraria from Aclaris, Celgene, Galderma, Genentech, LEO Pharma, Novartis, Ortho, Pfizer, Promius, Sanofi/Regeneron, and SunPharm. **Dr. Stein Gold** is an advisor and investigator for Foamix Pharmaceuticals Inc, Galderma, LEO Pharma, Novartis, and Valeant and is an investigator for Janssen, AbbVie, and Solgel. **Dr. Kircik** is an investigator and consultant for Foamix Pharmaceuticals. **Dr. Alexis** is a consultant for Beiersdorf, Bausch Health, Bristol Myers-Squibb, Celgene, Dermavent, Foamix, Galderma, LEO Pharma, L'Oreal, Menlo, Novartis, Pfizer, Sanofi-Regeneron, Scientis, UCB, Unilever, and Valeant; he reports grants and/or research support from Almirall, Bristol Myers-Squibb, Cara Therapeutics, Celgene, Galderma, LEO Pharma, Menlo, Novartis, and Valeant (Bausch Health). **Dr. Desai** is an investigator for Dermavant, AbbVie, Novan, and Symbio and a consultant for Pfizer, Foamix, Galderma, Scientis, Dermira, and Verrica. **Drs. Stakias** and **Stuart** are employees and stockholders at VYNE Therapeutics Inc.

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